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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,500	09/26/2005	Eberhard Amtmann	012627-041	7509

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EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
05/30/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/525,500	AMTMANN ET AL.	
	Examiner	Art Unit	
	WALTER E. WEBB	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Newly submitted claim 11 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

In reciting a method for the treatment of a cancerous disease in the originally filed claims, applicant has constructively elected this disease for examination on the merits. An autoimmune disease is distinct from a cancerous disease insofar as autoimmune diseases are not necessarily cancerous, such as diabetes, and as such would have been subject to a restriction requirement if previously presented.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 11 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of parvocellar bronchial or colorectal carcinoma, does not reasonably provide enablement for the treatment of cancerous disease in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

1)Scope of the disease being treated

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the predictability or unpredictability of the art;

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

6) the quantity of experimentation necessary;

7) the state of the prior art; and,

8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

Factors 1 and 2: The claimed invention is drawn to a method for the treatment of cancerous disease.

Factors 3 and 7: In particular, one skilled in the art could not practice the presently claimed subject matter without undue experimentation because the artisan would not accept on its face that the cancerous disease in general, could be effectively achieved by the administration of the claimed active agent.

The treatment of cancer with metal complexes is well known, but is unpredictable for the treatment of cancer in general. (See Salam Abu-Surrah et al., Current Medicinal Chemistry, 2006:13 at pg. 1338)

In this regard, Salam Abu-Surrah et al. is cited. Salam Abu-Surrah et al. discloses that cisplatin is one of the most successful anticancer metal complex, but despite it activity in many cancers, this compound is ineffective in others e.g. leukemia, renal and gastrointestinal cancers. They also disclose that new metal complexes including palladium instead of platinum are being developed. (See abstract and pp. 1349-1353.) However, given that cisplatin is limited in its treatment of cancer, the artisan would not expect applicant's compound to be able to treat cancerous diseases in general.

The Examiner acknowledges that the Office does not require the presence of working examples to be present in the disclosure of the invention (see MPEP §2164.02). However, in light of the state of the art, there is no apparent disclosure to support the contention that the treatment of cancerous disease in general can be achieved as claimed by applicant.

Factor 4: Applicant also disclosed how a human or animal might be administered this composition. Applicant did not disclose, for example, a protocol or guidance as to how the treatment of cancerous disease in general could be achieved. Applicant's disclosure is inadequate as to directing or guiding how the proposed agents can be employed to accomplish such objectives in a predictable manner.

Factor 5: The specification at pages 12-14 provides evidence demonstrating that a compound of formula I treats CALU-6 and SK-MEL *in vitro* and *in vivo* treatment of human small cell lung cancer (H10), for example. While the present claims encompass cancerous disease in general, Applicant's data merely establishes a treatment of only a handfull cancer types.

Factor 6: The burden of treating cancerous disease in general with a compound of formula I is much greater than that of treating parvocellar bronchial or colorectal carcinoma, with a specific compound. Since the present specification would not enable the skilled artisan to cancerous disease in general with the claimed compound, a clear burden of undue experimentation would be placed upon the artisan in order to practice the full scope of the presently claimed invention.

Factor 8: In view of the discussion of each of the preceding seven factors, the level of skill in this art is high and is at least that of a medical doctor with several years of experience in the art.

2) Scope of active agents

The specification does not adequately enable a person having ordinary skill in the art to use the claimed invention in light of the scope of palladium complexes claimed, where the residues can be a straight or branched alkenyl residue having 2-30 carbon atoms. There is no reasonable basis for assuming that myriads of compounds not made and thus not tested will share the requisite minimum activity needed to practice the invention. See In re Fisher, 166 USPQ 18, and In re Surrey, 151 USPQ 724 in regards to sufficiency of disclosure in cases directed to structure sensitive arts. The artisan would be faced with the impermissible burden of undue experimentation in determining which compound(s) showed sensitivity in treating a cancerous disease.

Summary

As the discussion of the above 8 factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the artisan with a reasonable expectation that the treatment of cancerous disease in general could be achieved. In order to actually achieve such an objective, it is clear from the discussion above that the skilled artisan could not rely on Applicant's disclosure as required by 35 U.S.C. § 112,

first paragraph. The artisan would be faced with the impermissible burden of undue experimentation in order to practice this embodiment of the claimed invention. Accordingly, claim 9 is deemed properly rejected.

Claim Rejections - 35 USC § 102

The rejection of claims 1-4 and 7 rejected under 35 USC 102(b) as being anticipated by Watt et al. is maintained. This rejection also applies to newly amended claim 12.

Applicant argues that Watt does not disclose pharmaceutical preparations and thus does anticipate the instant claims as currently amended. However, Watt does teach that the compounds are dissolved in ethanol, which is a pharmaceutically compatible diluent. Because the preparation involves mixing the compounds in ethanol, the reference also anticipates claim 12 now that this claim is complete as per MPEP § 2172.01. Accordingly, Watt anticipates the instant claims insofar as it teaches compounds of formula I and a pharmaceutically compatible diluent and a method of preparing the composition.

Claim Rejections - 35 USC § 103

Applicant's arguments, see pg. 9, lines 1-13, filed 2/21/2008, with respect to the rejection(s) of claim(s) 1-12 under 35 USC 103 (a) have been fully considered and are

persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made below.

Claims 5, 6 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watt et al. as applied to claims 1-4, 7 and 12 above, in view of Amtmann et al., (2002/0004526) and in further view of Das et al., (British Journal of Cancer 1978).

Watt and Amtmann, taught in the previous action, do not provide motivation to provide a palladium complex over a platinum complex. However, this motivation has been provided by Das et al. below.

Das et al. teach a comparison of cytotoxic action of some transitional metal chelates. (See pg. 466.) They compared the cytotoxic activity of nickel (Ni), palladium (Pd) and platinum (Pt). They found that nickel and palladium chelates showed superior cytotoxic activity to that of platinum. (See ibid.) They further added that palladium chelates are more likely to be effective anti-tumor agents than chelates of other metals. (See pg. 468, 1st paragraph.)

Applicant argues that Pd-preparations show seven to ten times higher effectiveness compared to the Pt-complexes disclosed in Amtmann and has better therapeutic potential since it has better solubility. Applicant also argues that the Pd-preparation has unexpected, significantly higher anti-tumor activity. However, these results are not unexpected in view of Das et al., which teach that palladium chelates are superior anti-tumor agents when compared to platinum chelates. Moreover, applicants results are not commensurate in scope with the instant claims insofar as applicants data

(IC_{50}-values at pH 6.8 of 0.6 and 0.8) shows support for the isopropyl residue of the Pd chelate, while the claims encompass a straight-chain or branched alkyl residue having 1-30 carbon atoms, for example.

Applicant admits that the kind of metal plays a critical role in the activity of the complexes and supports this admission with a cite from Freibolin et al. Freibolin further supports the teachings of Das et al. that palladium has superior anti-tumor effect than other metal complexes. Freibolin is later published as pointed out by applicant, but the notion that palladium is superior to platinum was well known before applicant's invention, as evidenced by Das et al. Therefore, it would have been obvious to a person having ordinary skill in the art at the time of applicant's invention to select palladium to make complexes superior to platinum and also use the compounds in the method taught in Amtmann.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612